

## REMARKS

The PTO states that Claims 1-16, 49-51 and 53-55 are pending. Claims 7-12 and 17-48 are cancelled. Applicants reserve the right to pursue all non-elected subject matter in one or more continuation, division or continuation in part applications. Applicants believe Claims 1-16 and 49-54 are pending. Applicants Request for Continued Examination of December 3, 2001, requested the entry of the amendment of July 5, 2001, including the entry of new Claims 52, 53 and 54. The subsequent Office Action of February 6, 2002, indicates that Claims 1-16 and 49-55 were pending. Applicants believe that Claims 52, 53 and 54 were erroneously entered as Claims 53, 54 and 55. After entry of Applicants Request for Continued Examination and this Amendment, Applicants believe Claims 1-16 and 49-54 are pending and under consideration.

### I. CLAIM REJECTION UNDER 35 U.S.C. § 103

Claims 1-6, 13-16, 49-51 and 53-55 stand rejected as allegedly obvious over Goldstein *et al.* (1993, *J. Cardiovasc. Pharmacol.* 22(2): 253-258) in view of Kataria *et al.* (1990, *J. Cardiothoracic Anesth.* 4/5 S2: 13-16). Applicants respectfully disagree. Neither Goldstein nor Kataria alone nor in combination teach or suggest each and every limitation of the rejected claims.

The PTO contends that there is no support on the record that patients undergoing bypass surgery were not extubated until up to 12-18 hours after surgery in 1993. Applicants submit herewith a Declaration under 37 C.F.R. § 1.132 of Dennis T. Mangano. Dr. Mangano is a physician and specialist in ischemic injury. Dr. Mangano attests to the state of the art in general anesthesia in 1993; specifically that patients having surgery under general anesthesia, circa 1993, such as in Goldstein, were generally not extubated until up to 12-18 hours after surgery.

The PTO also contends that one skilled in the cardiology art would have been motivated to administer a  $\beta_1$ -selective blocking agent to reduce cardiovascular complications following surgery. Dr. Mangano attests in the Declaration, that the use of  $\beta$ -blockers in surgical patients prior to, during surgery or immediately following surgery and daily thereafter was contraindicated prior to the filing of the above-identified application. Therefore one skilled in the art would not be motivated to administer a  $\beta$ -blocker to surgical patients prior to, during surgery or immediately following surgery and daily thereafter as

asserted by the PTO. Moreover, Dr. Mangano attests that those in the art did not consider the methods of the invention conventional. To the contrary, the state of the art at the time of filing of the subject application taught away from the present invention.

Dr. Mangano further attests that neither Goldstein nor Kataria teach or suggest administration of a pharmacologic cardiovascular agent prior to, during surgery or immediately after surgery and daily thereafter. Rather both Goldstein and Kataria teach administration of a  $\beta$ -blocker to patients after the emergence of sympathetic nervous system effects.

Applicants submit that neither Goldstein nor Kataria teach or suggest each and every limitation of the rejected claims. Applicants respectfully request that the rejection under 35 U.S.C. § 103 be withdrawn.

### CONCLUSION

Applicants submit that Claims 1-16 and 49-54 (or as provided by the PTO: Claims 1-6, 13-16, 49-51 and 53-55) satisfy all the criteria for patentability and are in condition for allowance. An early indication of the same is therefore kindly solicited.

Applicants believe no fee, other than the Petition for Time and Request for Continued Examination is due with this Amendment. However, pursuant to 37 C.F.R. §1.136 (a)(3), the Commissioner is authorized to charge all required fees, fees under 37 C.F.R. §1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds LLP, U.S. Deposit Account No. 16-1150 (Order No. 9114-004-999).

Respectfully submitted,

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